

Pneumocystis Lung Disease in Homosexual Men

These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California, San Francisco. Taken from transcriptions, they are prepared by Drs. David W. Martin, Jr, Professor of Medicine, and David G. Warnock, Associate Professor of Medicine, under the direction of Dr. Lloyd H. Smith, Jr, Professor of Medicine and Chairman of the Department of Medicine. Requests for reprints should be sent to the Department of Medicine, University of California, San Francisco, School of Medicine, San Francisco, CA 94143.

DR. SMITH:* *This Medical Staff Conference will be concerned with *Pneumocystis* lung disease in homosexual men. Dr. Jeffrey Golden will make the presentation.*

DR. GOLDEN:† In discussing *Pneumocystis carinii* pneumonia among gay men, I will concentrate on our experience here at the University of California and share with you what we are learning from our patients. Thus far, more questions than answers have been generated. I view this discussion as an interim exercise. We hope to better understand this peculiar and deadly epidemic in the near future. Also, I intend to make some basic comments about interstitial lung disease which I hope will enlighten you on the general topic of restrictive lung disease as well as that consequent to infection with *P carinii*.

Presentation of a Case

Let me begin with a patient who presented with *P carinii* pneumonia a little more than a year ago. He was a 43-year-old homosexual man who had been admitted in April 1981 because of increasing shortness of breath for one month. During the previous five months he had fever and diarrhea. Two

months before admission the diagnoses of amebiasis and giardiasis were made. One month before admission he was treated for syphilis. In the more distant past he had other diseases that we associate with his life-style, including hepatitis and shigellosis.

On physical examination, he was febrile. His respiratory rate was increased and his chest was clear to auscultation. Blood gas determinations done while the patient was breathing room air showed oxygen partial pressure (Po₂) 66, and carbon dioxide partial pressure (Pco₂) 37 mm of mercury and pH 7.47. Findings on x-ray studies of the chest done at the time of admission showed bilateral lower lobe interstitial infiltrates.

Initially we expected this process to be a "walking pneumonia," with a viral or *Mycoplasma* cause. The next day his oxygen tension dropped to the low 50's. We decided to do bronchoscopy and were very surprised by the transbronchial lung biopsy result. Examination of the specimen after hematoxylin and eosin staining showed alveoli filled with a proteinaceous eosinophilic material. This type of alveolar filling process is pathognomonic of *P carinii*. Silver methenamine stain showed the cyst stage of *P carinii*.

The patient was given sulfamethoxazole and trimethoprim (Septra). After eight days of treat-

*Lloyd H. Smith, Jr, MD, Professor and Chairman, Department of Medicine.

†Jeffrey Golden, MD, Assistant Clinical Professor of Medicine.

ment his shortness of breath, hypoxia and radiographic abnormalities cleared. The administration of the medication was discontinued after eight days because of leukopenia and a rash. He was sent home without any medicines and did perfectly well for four months. He was able to return to work and to walk the hills of San Francisco without complaints of shortness of breath. We thought that was the last we had seen of this patient.

Four months after his initial episode of *P carinii* pneumonia, he was seen again with a one-week history of shortness of breath. Findings on the chest x-ray film done on admission again showed bilateral lower lobe diffuse interstitial disease (Figure 1). On repeat transbronchial biopsy the diagnosis of *P carinii* pneumonia was made. This process worsened and during the next two days adult respiratory distress syndrome developed. The patient was put in the intensive care unit and given positive end-expiratory pressure. For the next three weeks he had an unrelenting downhill course. We witnessed, incidentally, the development of cor pulmonale in a period of two weeks. When a pulmonary artery line was placed at the time of admission to the intensive care unit, his pulmonary artery pressures were found to be normal. Two weeks later, with normal arterial oxygen tension maintained while receiving supplemental oxygen, his pulmonary artery pressures were as high as 80/40 mm of mercury. This interstitial lung process destroyed enough vasculature to cause pulmonary vascular hypertension in two weeks. An esophageal echocardiogram corroborated the diagnosis of cor pulmonale as manifested by a large right atrium and right ventricle and a small, slit-like left ventricle.

He was treated with pentamidine because of a recurrent rash after two days of taking sulfamethoxazole and trimethoprim. Repeat bronchoscopy was required to help decide whether or not we should continue pentamidine administration after two and three weeks of therapy. A bronchoscopic lavage of the patient's airways through his endotracheal tube was positive for *Pneumocystis* even after three weeks of pentamidine administration, just before he died. This tells us two things. First, one can carry out bronchoscopy safely through an endotracheal tube with positive end-expiratory pressure. In this context of a critically ill patient requiring positive airway pressure, we did a simple lavage. This is essentially a very expensive way of getting an induced sputum specimen. We

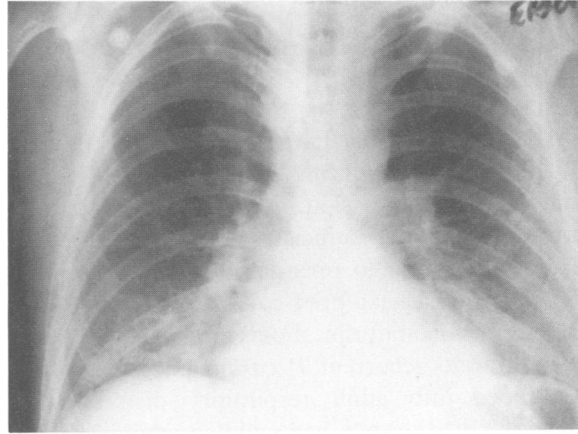


Figure 1.—X-ray film of the chest taken on the first day of patient's second University of California admission, showing classic interstitial infiltrates associated with *Pneumocystis carinii* pneumonia.

did not attempt a transbronchial biopsy for fear of causing a pneumothorax in the presence of positive airway pressure. Second, despite three weeks of pentamidine therapy, the *Pneumocystis* infection never cleared.

At autopsy small cysts were seen on the gross specimen of his lungs. The microscopic examination shows cysts alternating with areas of thickened, fibrotic alveolar walls. These cysts are also very evident on his last chest x-ray studies. We call these cysts "honeycombing." Honeycombing is the end stage of any severe interstitial process—*asbestosis*, *sarcoidosis*, *scleroderma* or *P carinii*, as in the case being discussed.

One month after the patient's initial episode of *P carinii* pneumonia, Dr. Arthur Ammann here at the University of California evaluated his immune status. At this time the patient was doing well and had normal immunoglobulin values. However, he was anergic on skin testing. His T-cell rosettes were decreased to 40 percent of his lymphocytes, instead of the expected 60 percent or greater. By monoclonal antibody assay the helper T cells were decreased to 7 percent; his suppressor T cells were increased to 65 percent, giving him a very low helper-to-suppressor cell ratio of 0.1. This ratio should be greater than 1.2. This low ratio implies almost no helper T-cell function. In addition, his lymphocytes did not function normally. When they were placed in mixed-lymphocyte culture or exposed to phytohemagglutinin, appropriate lymphocyte transformation was not evident. Even when he was well, this man had a severe quantitative and qualitative T-cell immunodeficiency. At this time we learned

that our colleagues in Los Angeles and New York were finding the same T-cell deficiency in homosexual patients who had *P carinii* pneumonia and Kaposi's sarcoma.

In summary, this first case was highly educational in that it taught us that gay men are at risk for immunosuppression. We also learned that bronchoscopy was sufficient to make a diagnosis without resorting to open-lung biopsy. This man did very well after a brief course of sulfamethoxazole and trimethoprim. Four months later, however, he had recurrent *P carinii* pneumonia that developed into adult respiratory distress from which he died despite pentamidine administration. As discussed, not only did he have interstitial fibrosis and honeycombing, the *P carinii* infection never cleared. Furthermore, cytomegalovirus was cultured from an autopsy lung specimen. The presence of concurrent cytomegalic infection has important implications in terms of the cause of this patient's state of severe immunosuppression.

Background

Let me say a word about the organism itself. *P carinii* was first discovered in 1909 by Chagas working with monkeys in Brazil.¹ He thought it was a developmental stage of *Trypanosoma cruzi*. The next year Carini found the organism in dogs and felt it was the schizogonic form of *Trypanosoma lewisi*. The first identification of this organism in human lungs was made by Van der Meer in the Netherlands in 1942. Vanek in 1952 established the causal relationship of *P carinii* and what was called interstitial plasma cell pneumonia of infants, which was epidemic during the socioeconomic collapse of Europe during and after World War II. In 1956 the first cases of *P carinii* pneumonia were found in this country.

The organism is a protozoan. It exists in two forms: a cyst form and a trophozoite form. One can only grow *Pneumocystis* in cell culture. It is very clear now that the disease is transmitted by inhalation. The trophozoite stage of *Pneumocystis* is inhaled and attaches to the alveolar lining epithelium. Pifer and co-workers² showed by phase-contrast microscopic observation of *P carinii* in chick epithelial lung culture that the trophozoite develops into a cyst form. The cyst matures and sporozoites develop within it. Subsequently, these sporozoites rupture out of the mature cysts and become trophozoites, and the cycle begins again.

P carinii is a ubiquitous organism. Studies at St. Jude's³ showed that 80 percent of healthy sub-

jects have significant titers to *P carinii* by the time they are 4 years old. This anti-*Pneumocystis* antibody is important in preventing disease from this ubiquitous infection. Masur and Jones⁴ showed that minutes after adding anti-*Pneumocystis* antibody to a preparation containing living alveolar macrophages, *Pneumocystis* trophozoites are phagocytized by macrophages. By electron microscopy the trophozoite can be observed to degenerate immediately upon contacting the macrophage vacuole. Just as we have humoral antibodies to this organism, our lymphocytes are also sensitized to *Pneumocystis*. In randomly selected subjects studied by Herrod and colleagues,⁵ 14 of 16 had lymphocytes that transformed spontaneously in the presence of *P carinii* cysts. Importantly, spontaneous transformation of lymphocytes by the *Pneumocystis* organism does not occur with naive umbilical cord blood. Evidently this protective mechanism must be acquired by prior inhalation of the organism.⁶

Despite a near universal exposure to this organism, our humoral and cellular immunity is very effective protection from disease. At St. Jude's, Perera and associates⁶ have shown that *P carinii* pneumonia develops only in people with immunosuppressive diseases or receiving immunosuppressive therapy. Perhaps more interesting, looking at 301 consecutive autopsies, they found 40 patients who had *Pneumocystis* infection in their lungs but did not have pneumonia. Of these 40 patients with inapparent *Pneumocystis* infection, 39 were immunosuppressed. Similarly, Hamlin⁷ found no *Pneumocystis* organisms in 245 consecutive autopsies done on patients dying without immunosuppressive diseases. Among 300 consecutive autopsies done on patients who had been severely immunosuppressed, however, *Pneumocystis* organisms in the lungs were identified in 14 (5 percent). Of these 14 cases, in only one was there associated pneumonia, the others having only inapparent infection. Presumably if these patients had lived longer or had more immunosuppressive chemotherapy, their inapparent infections may have developed into *Pneumocystis carinii* pneumonia. In fact, Perera's data do suggest that as one increases immunosuppressive chemotherapy in patients with leukemia, there exists a concomitant increase in the development of *P carinii* pneumonia. His leukemic patients given more immunosuppressive chemotherapy more frequently had clinical *Pneumocystis carinii* pneumonia and less frequently had inapparent

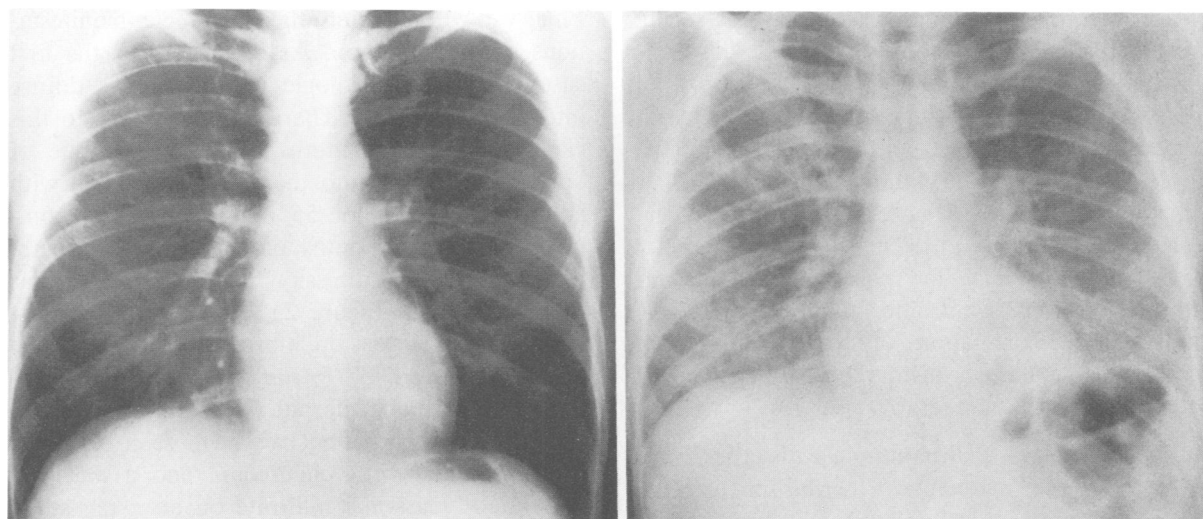


Figure 2.—Left, Normal chest x-ray study of a patient with an oxygen tension of 55 mm of mercury taken at the time a bronchoscopic examination that was positive for *Pneumocystis carinii* pneumonia. Right, X-ray film taken four days after initial normal film showing rapid progression of pneumonia.

Pneumocystis infection.⁶ Clearly, it is the immune status that relates to development of diseases from this ubiquitous organism.

Clinical Features

What are the clinical features of *P carinii* pneumonia? There is a basic philosophical point to make here. The clinical features of *P carinii* pneumonia are consistent and found in almost every case; unfortunately they are nonspecific. Patients present with dyspnea, fever and often cough. Physical findings include an average temperature elevation of 38.8°C. One may or may not hear inspiratory rales on pulmonary auscultation. The most impressive feature of Walzer's series of 116 patients with *P carinii* pneumonia was the average oxygen tension of 46 mm of mercury.⁸ In our series of patients we are finding cotton-wool exudates in the fundi, and this finding may be specific for *P carinii*. I should like to have Jim O'Donnell from our Department of Ophthalmology review some extraordinary eye findings in these patients.

DR. O'DONNELL:* We have been observing retinal cotton-wool spots in many gay male patients with unexplained immunosuppression. One such patient is a 34-year-old white man with a five-month history of fever, dry cough, dyspnea and weight loss. Funduscopic examination showed cotton-wool spots which existed in the presence of clear ocular media and normal retinal vessels. There

was no evidence of ischemic retinal vascular disease such as hypertension or diabetes. These were actually cotton-wool spots by the jargon of ophthalmology, not exudates. They are infarctions in the nerve fiber layer which is on the superficial retina. The feathery edges are the nerve fiber layer itself. Despite therapy with sulfamethoxazole with trimethoprim as well as pentamidine, the patient died. At autopsy, light microscopy showed areas of nerve fiber layer degeneration and cytoid bodies. There was nonspecific staining with silver methenamine. Transmission electron microscopy, however, showed cyst forms of *Pneumocystis*. The *Pneumocystis* were seen in the ganglia and inner plexiform layers of the retina, adjacent to retinal vessels in the vicinity of the cotton-wool spots.

Extrapulmonary dissemination in *Pneumocystis* infection is rare, although the organism has been reported in lymph nodes, spleen, liver, peripheral blood, myocardium, stomach, small intestine, bone marrow, adrenal gland and thyroid. This is the first demonstration of *Pneumocystis* in the eye. It has not yet been found in the brain. The pathophysiology of this is obscure, but these organisms in the retina may cause focal nerve fiber layer infarctions which clinically manifest as the cotton-wool spots. There are many causes of cotton-wool spots, of course, and cotton-wool spots should not be regarded as pathognomonic for *Pneumocystis*. In terms of the current epidemic of unexplained immunosuppression in gay men, it is my clinical impression based on a limited number of patients that we are seeing cotton-wool spots in patients

*James J. O'Donnell, MD, Assistant Professor of Ophthalmology.

with *P carinii* pneumonia but we are not seeing them in patients with Kaposi's sarcoma. The clinical significance of this finding is that cotton-wool spots may be an important sign in patients with suspected *Pneumocystis*. The presence of cotton-wool spots in gay men without evidence of other ischemic retinal disease, such as diabetes or hypertension, should alert physicians to the possibility of *Pneumocystis* and the possibility of the immunosuppression syndrome. We are currently studying the correlation of these cotton-wool spots with the natural history of the disease and with the response to therapy.

DR. GOLDEN: We shall continue with other clinical aspects of *Pneumocystis carinii* pneumonia.

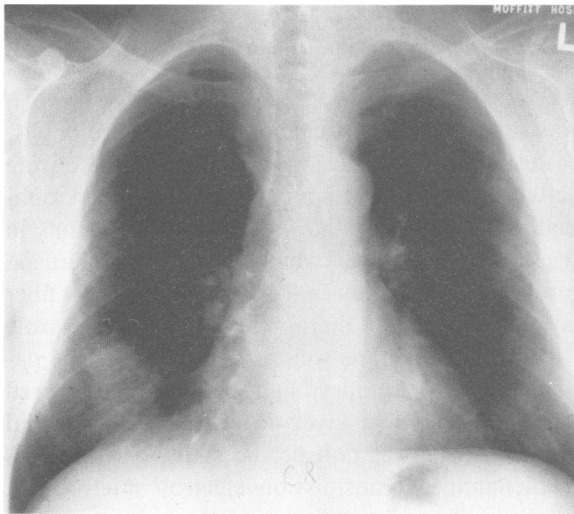


Figure 3.—X-ray study of the chest of a renal transplant patient with a localized infiltrate that proved to be *Pneumocystis carinii* on bronchoscopy.

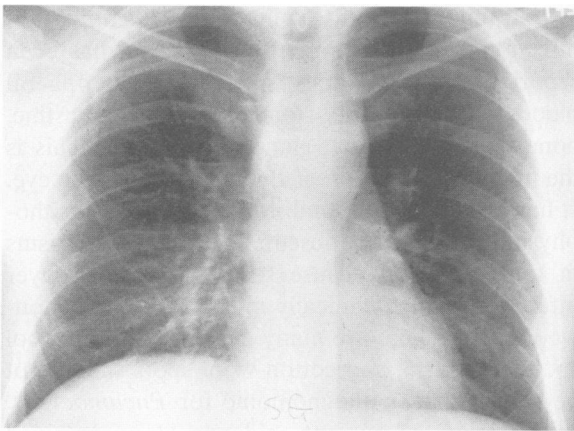


Figure 4.—X-ray study of the chest showing diffuse infiltrates that proved to be pulmonary Kaposi's sarcoma on bronchoscopy and subsequent autopsy evaluation.

First we will mention the radiologic manifestations of this infection. As described for the first case, the usual radiologic presentation is diffuse interstitial infiltrates. There are exceptions to this classic radiologic pattern. For example, one of our patients came into the emergency room with an oxygen tension of 55 mm of mercury, complaining of two months of shortness of breath. Surprisingly, his admission chest x-ray film was entirely normal (Figure 2). Given his social history and oxygen tension, a bronchoscopy was done and a diagnosis of *Pneumocystis carinii* pneumonia was made despite normal chest x-ray studies. Another patient we have seen this past year presented with pneumonia and a localized nodular or mass-like infiltrate on an x-ray study of the chest (Figure 3) six months after a renal transplant. This localized lesion proved to be *Pneumocystis carinii* pneumonia by bronchoscopy. Incidentally this patient was not gay. We now recognize that the radiologic presentation of *Pneumocystis carinii* has to be broadened to include even x-ray films that show no abnormalities and those showing localized abnormalities, not just diffuse interstitial disease.

How does one make the diagnosis of *Pneumocystis carinii* pneumonia? Uncommonly, the organism can be found in the sputum. Usually one has to rely on invasive techniques. We have found bronchoscopy to be 100 percent effective in diagnosing this disease. Open lung biopsy has been unnecessary. As of this conference, we have diagnosed *Pneumocystis carinii* pneumonia in seven gay patients with T-cell abnormalities and interstitial lung disease. We have been effective in ruling out *Pneumocystis carinii* pneumonia with bronchoscopy in four gay patients with T-cell abnormalities and interstitial lung disease. How do we know they are bronchoscopic true negatives? None of the four have gone on to show any changes consistent with *Pneumocystis carinii* pneumonia in months of follow-up. Instead, we have made bronchoscopic diagnosis of cytomegalovirus as the cause of their interstitial lung disease. In one gay man with known Kaposi's sarcoma, T-cell defects and radiologic evidence of interstitial disease (Figure 4), we diagnosed pulmonary Kaposi's sarcoma by transbronchial biopsy.

Cases Being Followed

One of the most basic questions that has arisen from this epidemic is how best to follow cases of

patients with previous *P. carinii* pneumonia who are out of the hospital and doing well. As the initial case presentation illustrates, these patients must be observed for early signs of deterioration. At this point it is not clear which test—screening pulmonary function (lung volumes, airflow rates, diffusing capacity), exercise physiology, gallium lung scan, T-cell function and the like—should be done and how often. The answer to the related question of which test might be an effective screening device to detect the early manifestations of this type of pneumonia in the susceptible population also is not known.

We are now following in our outpatient department five homosexual patients with previous *Pneumocystis carinii* infection. I will present one of these cases as an example of how we are approaching the issue of appropriate follow-up. A 45-year-old gay man presented to the emergency room in October 1981 after two weeks of shortness of breath. On examination he was febrile and he had interstitial rales, thrush and an herpetic penile lesion. An x-ray study showed interstitial infiltrates and oxygen tension was 44 mm of mercury. After bronchoscopy the diagnosis of *Pneumocystis carinii* pneumonia was made. Despite intravenous administration of sulfamethoxazole with trimethoprim his pulmonary process progressed to adult respiratory distress syndrome. Given supplemental oxygen and positive end-expiratory pressure therapy, he began to improve slowly over a two-week period. He was discharged from the hospital two weeks later with dramatic clinical and radiologic clearing of his life-threatening pneumonia. Thinking back to our first patient who did well for four months only to die because of recurrent *Pneumocystis carinii* pneumonia, we wondered whether serial pulmonary function tests would be an effective way to follow his pulmonary status, especially in order to detect early signs of deterioration. His initial screening pulmonary function showed all three criteria of significant interstitial lung disease. First, all of his lung volumes were reduced, or "restricted," significantly below normal. Second, the diffusing capacity for carbon monoxide, a test for the intactness of the alveolar capillary bed, was reduced. Third, he had high airflow rates assessed by both forced expiratory volume in one second and maximal expiratory flow volume curves. High flow rates are typical of interstitial pulmonary disease and may result from high recoil pressure characteristic of stiff, noncompliant lungs. His small or

restricted lung volumes, low diffusing capacity and high flow rates are consistent with his severe interstitial lung infection.

For the six months since discharge, he has been completely free of symptoms and has returned to work. He could not tolerate sulfamethoxazole with trimethoprim therapy because of a rash. He has been given monthly pooled immunoglobulin intravenously because we have detected humoral immunity dysfunction in terms of his response to pneumococcal vaccine. Finally, he has been sexually abstinent since discharge. His screening pulmonary function tests have shown slow but dramatic return to normal over this six month period. We are carefully observing his lung function to see if a subtle decrease in lung volumes or diffusing capacity might be a harbinger of recurrent *Pneumocystis carinii* pneumonia.

This patient has also had his pulmonary physiology assessed during exercise. We now know that a clear chest x-ray film⁹ and so-called "normal" screening pulmonary function tests do not rule out the presence of significant interstitial lung disease. For this reason we undertake exercise pulmonary function testing to detect the presence of an underlying interstitial process in suspicious settings. Incidentally, it is now possible to show physiologic evidence of asbestosis with exercise testing in persons exposed to asbestos who complain of dyspnea on exertion but in whom screening pulmonary function test results are normal at rest.

This patient's exercise test was done on a bicycle ergometer with simultaneous collection of expired gases and arterial blood. In interstitial lung disease one expects an abnormal pattern of ventilation and gas exchange as the work load is progressively increased. Such patients hyperventilate primarily by increasing respiratory rate while maintaining small tidal volumes. This inappropriate hyperventilation is due to hypoxia, presence of a large dead space or, most important, a neural reflex arising in the distal lung parenchyma. In terms of gas exchange, a fall in oxygen tension and an increase in alveolar-arterial oxygen difference with the stress of exercise will develop in patients with interstitial lung disease even with normal resting arterial blood gas values. In contrast, in this patient results of an exercise test four months after his near fatal *Pneumocystis carinii* pneumonia were normal. His ventilation increased in a normal pattern with increasing exercise levels. Furthermore, his oxygen tension

was normal with each exercise level. Currently, this patient has normal pulmonary function at rest and with exercise. We will be conducting serial exercise tests with ear oximetry to follow this case. The development of abnormal hyper-ventilation with exercise may be an indicator of early clinical deterioration.

We are also evaluating gallium lung scans as another way to follow our patients with previous *Pneumocystis carinii* pneumonia. Findings on this patient's gallium lung scan now are normal and thus correlate with his normal exercise function. Two other similar outpatients still have positive gallium scans and repeat bronchoscopy in these two patients shows persistent *P. carinii*. Thus our evaluation still shows *Pneumocystis carinii* pneumonia despite the absence of dyspnea on exertion. We shall continue to observe these patients using screening and exercise pulmonary function tests, gallium scans, bronchoscopy and T-cell functional studies to evaluate the effectiveness of treatment and early detection of clinical deterioration.

Summary of Cases

In summary, we have had eight gay patients present with *Pneumocystis carinii* infection. All the patients were white and male, and the age range was 31 to 46 years. Every patient's transbronchial biopsy specimen grew out cytomegalovirus. All had T-cell dysfunctions identical or similar to those of the first patient presented. The clinical courses of these patients have varied. Two patients had two episodes of pneumonia separated by many months. Both died after the second episode. One patient presented with mild shortness of breath and died after a rapid two-week downhill course. We now are observing five patients receiving various types of therapy, including administration of sulfamethoxazole with trimethoprim, immunoglobulin, thymosin and so forth. They are doing well clinically at this point.

Possible Causes

I would like to conclude with a discussion of the possible mechanisms of the immunosuppression that is central to this epidemic. First, we are not "reinventing the wheel"; this is a new phenomenon. True, *Pneumocystis carinii* and Kaposi's sarcoma are not new entities, but the immunosuppression in young gay men is certainly new. Why are these patients losing immune function? In a recent *Morbidity and Mortality Report* from the Centers for Disease Control, cases of 13 gay

men with either Kaposi's sarcoma, *Pneumocystis* or both are presented.¹⁰ Of these 13 patients, nine had recent, definite, direct sexual contact with other patients with either Kaposi's sarcoma or *Pneumocystis carinii* pneumonia before *Pneumocystis* pneumonia or Kaposi's sarcoma developed. Furthermore, of the six patients with Kaposi's sarcoma, in three the disease developed after sexual contact with patients known to have Kaposi's sarcoma.¹⁰ This suggests that either there is something causal about their shared life-style or there is an infection being transmitted among members of this particular small cluster. What aspects of their shared life-style could contribute to immunosuppression? Obviously, drugs are a consideration. Marijuana, for example, has been shown to cause some T-cell problems in otherwise "normal" people.¹¹ Given the level of marijuana use in the San Francisco Bay Area, I think if marijuana were a significant cause of immunosuppression, the Immunology Clinic here at the University of California would have to meet in a football stadium. What are the other possibilities? Amyl nitrite is a drug of more recent popularity for its ability to heighten orgasm. In a recent article in *The Lancet*, researchers at the National Institute of Health reported that amyl nitrite, itself, can cause immunosuppression.¹² However, many of the patients in this series had "gay lymph node syndrome," or previous cytomegalovirus infection shown by serology, or both. This complicates interpretation of the effect of this drug on the immunosuppression syndrome.

If the recently reported clustering of cases in Southern California is confirmed, another possible cause of this epidemic immunosuppression is infection. In this context, a most likely candidate is cytomegalovirus. Here in San Francisco, Dr. W. Lawrence Drew showed that almost all homosexual men have positive serologies to cytomegalovirus. Furthermore, he also showed that 14 percent of gay men had this virus in their urine. This is based on only single urine samples. Perhaps if more than one sample were cultured, the virus might be isolated at an even higher frequency. No heterosexual patient in his series had a positive urine culture for cytomegalovirus.¹³ In terms of the gay life-style, cytomegalovirus has particular relevance. First, we know that it can remain in the semen of an infected man for well over a year. This prolonged asymptomatic presence in semen undoubtedly relates to venereal transmission of the virus.¹⁴ Furthermore, there are

significant immunologic sequelae due to cytomegalovirus infection. For example, it is the cause of the common mononucleosis syndrome in up to 20 percent of cases. In subjects who have this mild illness due to cytomegalovirus there is an acute T-cell dysfunction as severe as in our gay patients with *Pneumocystis carinii* pneumonia.¹⁵⁻¹⁸ In addition, there is some experimental animal evidence that the severity of the immunosuppression is directly related to the size of the virus inoculum.¹⁹ After some months, patients with previous cytomegalovirus mononucleosis have a return toward normal of their immune function. In the context of our gay patients there are at least two possibilities in terms of cytomegalovirus-induced immunosuppression. First, there may be a new particularly virulent strain of the virus being spread among a few homosexual men. Second, gay men may be experiencing so much repeated contact with semen containing this virus that they are having serial acute cytomegalovirus-induced immunosuppressive infections from which they remain permanently immunoincompetent.

Kaposi's sarcoma is a part of this epidemic, and there is a clear relationship between this tumor and cytomegalovirus. By electron microscopy, the virus has been found in Kaposi's sarcoma specimens.²⁰ In addition, portions of the virus genome have been identified in the genetic material of Kaposi's sarcoma.²¹ Kaposi's sarcoma is felt to be a tumor that occurs in the setting of immunosuppression such as among renal transplant patients.²² Cytomegalovirus, by causing a state of immunosuppression, could be causally related to the development of Kaposi's sarcoma. In my view, just as *Pneumocystis carinii* pneumonia is an opportunistic infection, I think it is clear that Kaposi's sarcoma is an opportunistic tumor. Perhaps both

tumor and infection result from cytomegalovirus infection.

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